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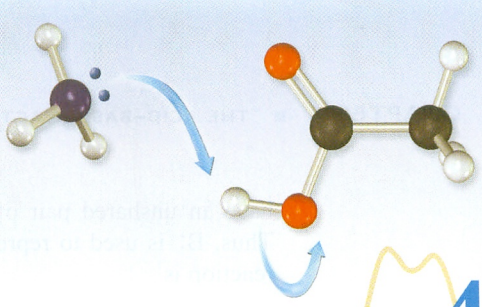

The Acid–Base Reaction

CHAPTER 4

THIS CHAPTER provides our first detailed examination of a chemical reaction, the acid–base reaction or transfer of a proton. Although acid–base reactions are simple, they are very important in organic chemistry because more complicated reactions often involve one or more proton transfer steps. In addition, an important purpose of this chapter is to introduce many concepts about reactions in general. Much of what we learn about the acid–base reaction is applied to other reactions in later chapters.

Acid–base reactions are equilibria, so the concept of equilibrium is reviewed. The rates of these reactions are also discussed. The largest part of the chapter is a discussion of how the structure of the acid or base affects its acid or base strength. We will learn to predict what happens to the strength of an acid when its structure is changed. Not only does this help us to remember how strong an acid (or base) is and how to estimate the strength of an acid or base we have not seen before, but it is of additional importance because exactly the same reasoning is used in later chapters to predict the effects of structural changes on the rates and equilibria of other reactions.

MASTERING ORGANIC CHEMISTRY

- Writing Equations for Acid–Base Reactions
- Recognizing Lewis Acids and Bases
- Understanding the Acid–Base Equilibrium
- Understanding the Factors That Affect the Strength of Acids and Bases
- Predicting the Relative Strengths of Acids and Bases
- Identifying the Most Acidic Proton in a Compound

4.1 DEFINITIONS

There are several definitions of acids and bases. According to the **Bronsted-Lowry definition,** an **acid** is a proton donor and a **base** is a proton acceptor. Any compound that has a hydrogen can potentially act as a Bronsted-Lowry acid (although the strength of the acid can vary enormously). Therefore, H—A is used as a general representation for an acid. To accept a proton, most bases

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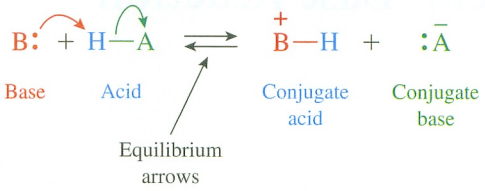
have an unshared pair of electrons that can be used to form a bond to the proton. Thus, B: is used to represent a general base. The general equation for an acid–base reaction is



Important Convention

In this reaction, a proton is transferred from the acid to the base. The unshared pair of electrons on the base is used to form the new bond to the proton while the electrons of the H—A bond remain with A as an unshared pair. *Previously, curved arrows have been used to show electron reorganization in resonance structures. Organic chemists also use these arrows to show electron movement in reactions. The arrows are a kind of bookkeeping device that helps us keep track of electrons as the Lewis structures of the reactants are converted to the Lewis structures of the products. Remember, an arrow always points from where the electrons are to where they are going. It does not point from where the hydrogen (or other atom) is to where it is going.*

PRACTICE PROBLEM 4.1

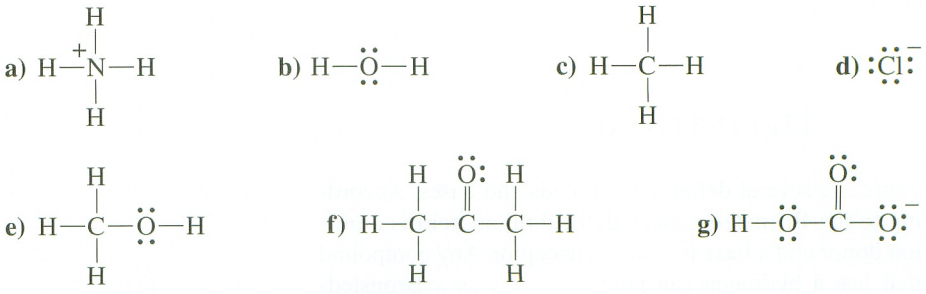
Explain whether ammonia, NH_3, can act as an acid, a base, or both.

Solution

Because NH_3 contains hydrogens, it can act as an acid, and because it has an unshared pair of electrons, it can act as a base. We tend to think of it as a base because that is how it reacts with water. However, in the presence of a strong base, NH_3 can react as an acid. Because many organic reactions involve strongly basic reagents, we need to be aware of the potential of any hydrogen-containing species to donate a proton.

PROBLEM 4.1

Indicate whether each of these species can act as an acid, a base, or both:



Acid–base reactions are reversible or equilibrium processes. In the reverse reaction, BH^+ acts as the acid and A^- is the base. Therefore, BH^+ is called the **conjugate acid**

of the base B, and A^- is the **conjugate base** of the acid HA. The charges in a specific acid–base reaction may be different from those shown in the preceding general equation. The proton is positive, so one unit of positive charge is transferred from the acid to the base in the reaction. The initial charge of HA and B can vary, but B is always one unit more negative than BH and HA is always one unit more positive than A.

PROBLEM 4.2

Show the conjugate acids of these species:

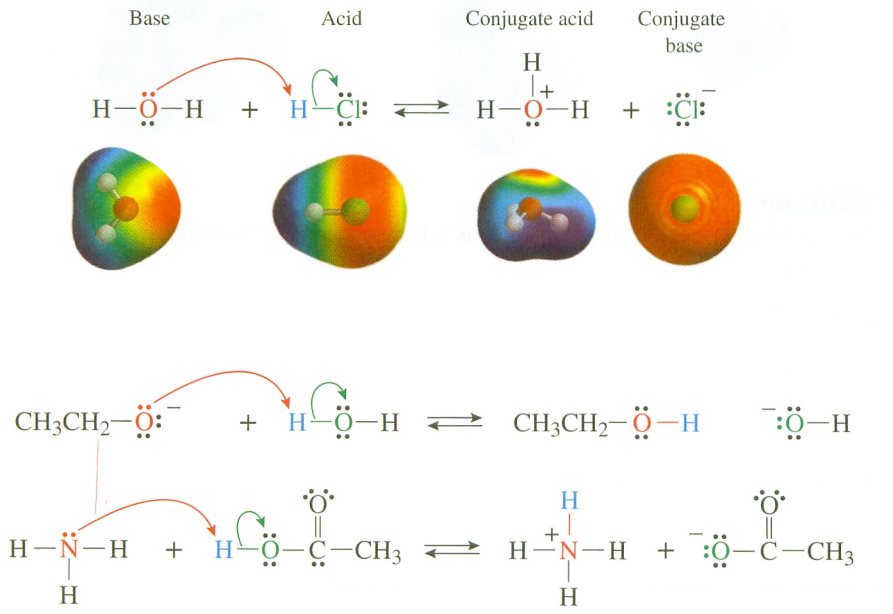
a) $CH_3-\ddot{O}-H$ **b)** $H-\ddot{O}:^-$ **c)** $CH_3-\ddot{N}H_2$

PROBLEM 4.3

Show the conjugate bases of these species:

a) $H-\ddot{O}-H$ **b)** $H-\overset{+}{\ddot{O}}(H)-H$ **c)** $H-\ddot{N}(H)-H$ **d)** $H-C(H)(H)-C(H)(H)-H$

Note that a compound that has both a hydrogen and an unshared pair of electrons can potentially react as either an acid or a base, depending on the reaction conditions. Water, ammonia, and alcohols are examples of compounds that react as acids in the presence of strong bases and as bases in the presence of stronger acids. Some specific examples of acid–base reactions are shown in Figure 4.1. Water is the base in the first equation and the acid in the second equation.



Active Figure 4.1 ORGANIC Chemistry Now™

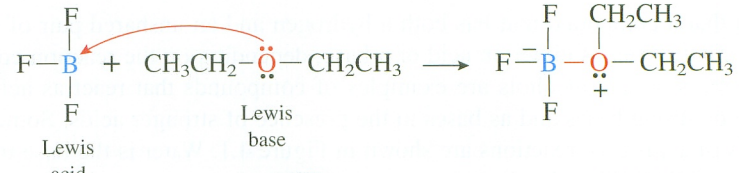
SOME ACID–BASE REACTIONS. Test yourself on the concepts in this figure at **OrganicChemistryNow.**

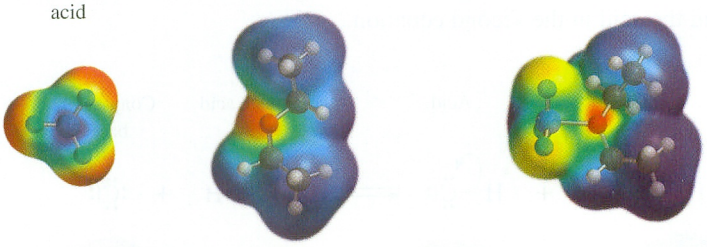
PROBLEM 4.4

Complete these acid–base equations. Use the curved arrow method to show the electron movement in the reactions.

	Base	Acid	Conjugate acid	Conjugate base
a)	$:\ddot{N}H_2^-$	$+ H_2\ddot{O}:$	$\rightleftharpoons$	
b)	$CH_3\ddot{O}:^-$	$+ H_3O:^+$	$\rightleftharpoons$	

According to the **Lewis definition,** an acid is an electron pair acceptor and a base is an electron pair donor. All Bronsted-Lowry bases are also Lewis bases. However, Lewis acids include many species that are not proton acids; instead of H^+, they have some other electron-deficient species that acts as the electron pair acceptor. An example of a Lewis acid–base reaction is provided by the following equation. In this reaction the boron of BF_3 is electron/deficient (it has only six electrons in its valence shell). The oxygen of the ether is a Lewis base and uses a pair of electrons to form a bond to the boron, thus completing boron's octet.





PROBLEM 4.5

Indicate whether each of these species is a Lewis acid, a Lewis base, or both:

a) $H-\overset{H}{\underset{H}{\overset{|}{\underset{|}{C^+}}}}$ b) $H-\ddot{O}-H$ c) $H-\overset{H}{\underset{H}{\overset{|}{\underset{|}{B}}}}$

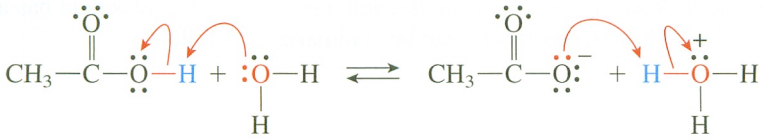
d) $CH_3-\overset{H}{\underset{H}{\overset{|}{\underset{|}{N}}}}-H$ e) $:\ddot{Cl}-\overset{:\ddot{Cl}:}{\underset{:\ddot{Cl}:}{\overset{|}{\underset{|}{Al}}}}$

To avoid confusion, when the term *acid* or *base* is used in this text, it refers to a proton acid or base—that is, a Bronsted-Lowry acid or base. The term *Lewis acid* or *Lewis base* will be used when the discussion specifically concerns this type of acid or base.

4.2 THE ACID–BASE EQUILIBRIUM

The reaction of an acid with a base is in equilibrium with the conjugate base and conjugate acid products. The equilibrium constants, termed *acid dissociation* or *acidity constants,* for the reactions of many acids with water as the base (and solvent) have been determined. They can be found in various reference books. Some selected acidity constants are listed in Table 4.2 in Section 4.9. Let's see how acidity constants are defined.

Consider the following acid–base equilibrium, the ionization (dissociation) of acetic acid in water:



The equilibrium constant for this reaction is

$$K = \frac{[CH_3CO_2^-][H_3O^+]}{[CH_3CO_2H][H_2O]}$$

Because water is also the solvent, it is present in large excess, and its concentration is approximately constant during the reaction. Therefore, a new equilibrium constant, the **acidity constant** (K_a), is used. For the preceding reaction the equation for K_a is

$$K_a = K[H_2O] = \frac{[CH_3CO_2^-][H_3O^+]}{[CH_3CO_2H]} = 1.8 \times 10^{-5}$$

The acidity constant is a measure of the strength of an acid. If the acidity constant for a particular acid is near 1, about equal amounts of the acid and its conjugate base are present at equilibrium. A strong acid, which dissociates nearly completely in water, has an acidity constant significantly greater than 1. A weak acid, which is only slightly dissociated in water, has an equilibrium constant significantly less than 1. The acidity constant for acetic acid is 1.8×10^{-5}—only a small amount of acetic acid actually ionizes in water. It is a weak acid.

The acidity constants that are encountered in organic chemistry vary widely, from greater than 10^{10} to less than 10^{-50}. Because of this wide range, it is convenient to use a logarithmic scale to express these values, as is done with pH. Therefore, pK_a is defined as

$$pK_a = -\log K_a$$

PRACTICE PROBLEM 4.2

If the pK_a of a compound is 10, what is its K_a?

Solution

The calculation is easy when pK_a is an integer. If pK_a = integer, then $K_a = 1 \times 10^{-\text{integer}}$. So if $pK_a = 10$, $K_a = 1 \times 10^{-10}$. It is also easy to go in the reverse direction when $K_a = 1 \times 10^x$ because then $pK_a = -x$.

PROBLEM 4.6

Provide the values for the missing K_a or pK_a in the following examples:

a) $pK_a = -4$; $K_a = ?$

b) $K_a = 1 \times 10^{-16}$; $pK_a = ?$

c) $pK_a = 38$; $K_a = ?$

d) $K_a = 1 \times 10^{6}$; $pK_a = ?$

It is important to be able to quickly recognize the strength of an acid from its K_a or pK_a value. As the strength of the acid increases, the K_a increases and the pK_a decreases (becomes more negative). Base strengths can be determined from the K_a (or pK_a) of the conjugate acid. A strong acid has a weak conjugate base, and a weak acid has a strong conjugate base. These relationships can be summarized as follows:

Strong acid	$K_a > 1$	Negative pK_a	Weak conjugate base
Weak acid	$K_a < 1$	Positive pK_a	Strong conjugate base

PROBLEM 4.7

Indicate whether these compounds are weaker or stronger acids than water (the K_a for water is 1.8×10^{-16}; the pK_a is 15.74):

a) $HClO_4$ ($K_a = 10^{10}$) **b)** $HC{\equiv}CH$ ($pK_a = 25$)

c) $HOCOH$ ($pK_a = 6.35$) **d)** CH_3CH_3 ($K_a = 10^{-50}$)

PROBLEM 4.8

Indicate whether these species are weaker or stronger bases than hydroxide ion. The K_a or pK_a values are for the conjugate acids.

a) $:\ddot{N}H_2^-$ ($K_a = 10^{-38}$) **b)** $CH_3CH_2\ddot{C}H_2^-$ ($pK_a = 50$)

c) $\ddot{N}H_3$ ($pK_a = 9.24$) **d)** $:\ddot{C}l:^-$ ($pK_a = -7$)

Consider the general acid–base reaction (charges omitted)

$$H{-}A + B: \rightleftharpoons A: + H{-}B$$

The equilibrium constant (K) for this reaction is

$$K = \frac{K_a \text{ (for HA)}}{K_a \text{ (for HB)}}$$

If HA is a stronger acid than HB, then K is greater than 1 and the right-hand side of the equation is favored at equilibrium; that is, the concentrations of the products (A and

HB) are greater than the concentrations of the reactants (HA and B). If HB is a stronger acid than HA, then K is less than 1 and the equilibrium lies to the left. In general, *the equilibrium favors the formation of the weaker acid and the weaker base.* (Because the stronger acid has the weaker conjugate base, the weaker base is always on the same side of the equation as the weaker acid.)

As an example, consider the following reaction:

$$H{-}Br + H_2O \rightleftharpoons Br^- + H_3O^+$$

HBr is a stronger acid ($K_a = 10^9$ or $pK_a = -9$) than H_3O^+ ($K_a = 55$ or $pK_a = -1.74$), so this equilibrium lies to the right. From the K_a's the equilibrium constant for the reaction can be calculated to be 1.8×10^7. This equilibrium constant is so large that the amount of HBr remaining cannot be measured by most experimental techniques. For all practical purposes the equilibrium lies completely to the right. Strong acids, such as HBr, are said to be completely dissociated in water. Differences in the strengths of very strong acids cannot be detected in water. Equilibrium constants as large as the one for the reaction of HBr with water cannot be measured directly and must be determined by some indirect means. Therefore, the pK_a values of the very strong acids (and also the very weak acids) listed later in Table 4.2 are only approximate. However, they are usually accurate enough for predictions to be made about the position of the equilibrium in an acid–base reaction.

Figure 4.2 shows a scale of the strengths of some of the acids commonly encountered in organic chemistry. At the left side of the scale are *strong acids* such as perchloric ($HClO_4$), hydrobromic (HBr), and sulfuric (H_2SO_4) acids, all of which are significantly stronger than H_3O^+ and are completely ionized in water. Acids that are stronger than H_2O but weaker than H_3O^+ are partially dissociated in water and are

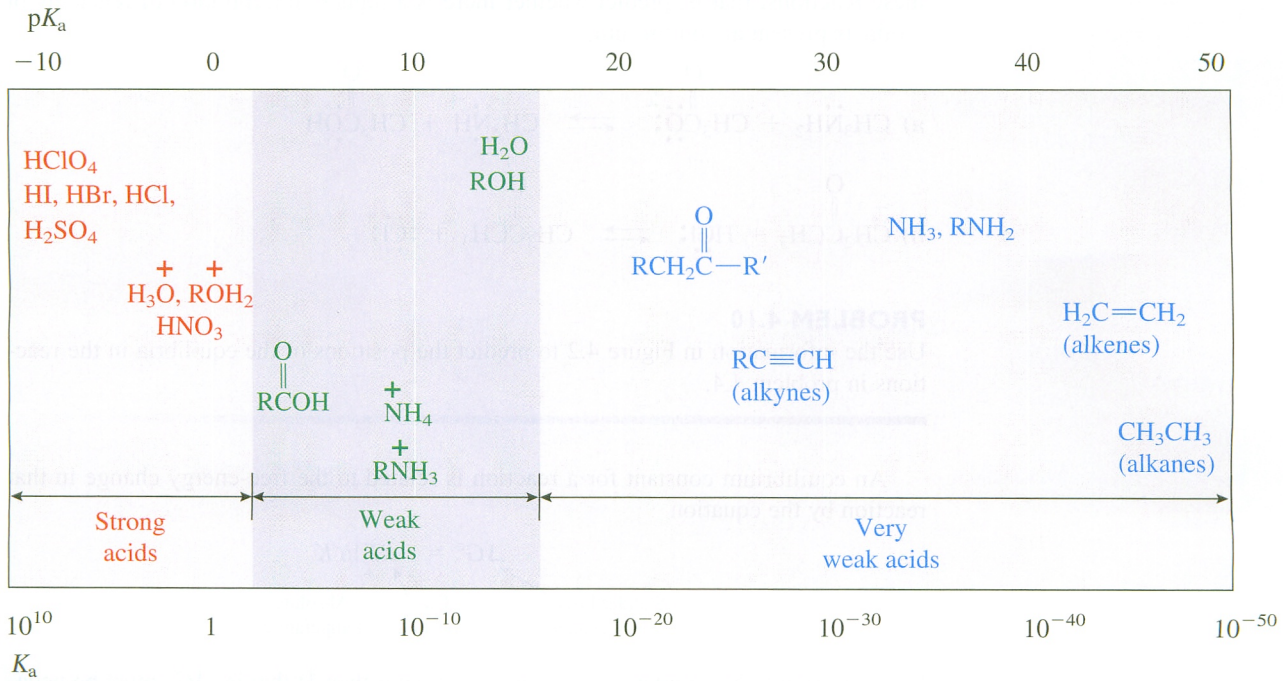


Figure 4.2

SCALE SHOWING SOME ACID STRENGTHS.

termed *weak acids* in this text. Included in this group are carboxylic acids and the conjugate acids of ammonia and the amines. Acids that are comparable to or weaker than H_2O are essentially undissociated in water and are termed *very weak acids.* However, they can react as acids in the presence of very strong bases in solvents that are less acidic than water. The majority of organic compounds fall into this group, ranging from alcohols (pK_a's about 16), which are similar in acid strength to water, to aldehydes and ketones (pK_a's about 20), which are a little less acidic than water, to alkanes (pK_a's about 50), which are extremely weak acids.

PRACTICE PROBLEM 4.3

Use Figure 4.2 to predict whether the reactants or the products of this reaction are favored at equilibrium:

$$CH_3\ddot{C}H_2^- + HC{\equiv}CH \rightleftharpoons CH_3CH_3 + HC{\equiv}C:^-$$

Solution

From Figure 4.2, HC≡CH is a stronger acid than CH_3CH_3. Because the equilibrium favors the weaker acid, more of the products are present when this reaction reaches equilibrium.

PROBLEM 4.9

Using the information available in Figure 4.2, predict the position of the equilibrium in these reactions; that is, predict whether there is a higher concentration of reactants or products present at equilibrium:

a) $CH_3\ddot{N}H_2 + CH_3\overset{\overset{O}{\|}}{C}\ddot{O}:^- \rightleftharpoons CH_3\ddot{N}H^- + CH_3\overset{\overset{O}{\|}}{C}\ddot{O}H$

b) $\ddot{C}H_2\overset{\overset{O}{\|}}{C}CH_3 + H\ddot{C}l: \rightleftharpoons CH_3\overset{\overset{O}{\|}}{C}CH_3 + :\ddot{C}l:^-$

PROBLEM 4.10

Use the information in Figure 4.2 to predict the positions of the equilibria in the reactions in problem 4.4.

An equilibrium constant for a reaction is related to the free-energy change in that reaction by the equation

$$\Delta G^\circ = -RT \ln K$$

Standard free energy change; Gas constant; Absolute temperature

For a reaction to be spontaneous, K must be greater than 1; that is, ΔG° must be negative. Organic chemists find diagrams that show the free energies of the reactants and

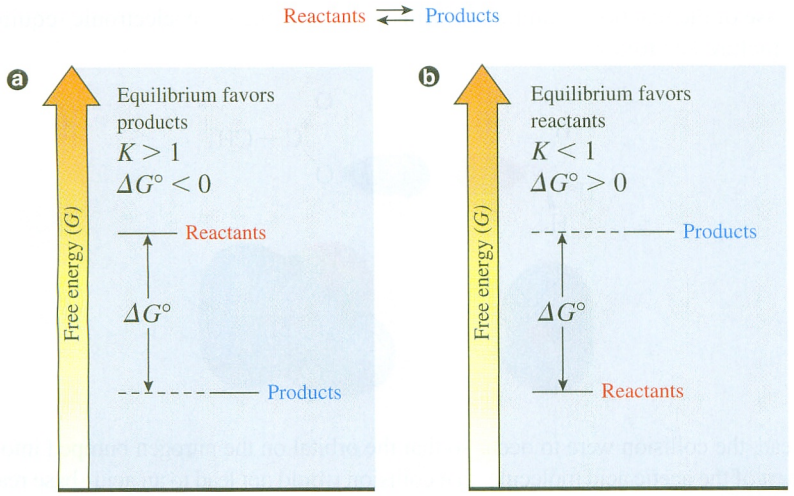


Figure 4.3

FREE ENERGIES OF REACTANTS AND PRODUCTS. (a) The products are more stable than the reactants and are favored at equilibrium. (b) The reactants are more stable and are favored.

products on the same scale to be very useful. Figure 4.3 shows such diagrams for two general reactions. In the diagram on the left-hand side of this figure, the reactants are higher in energy than the products. Therefore, $\Delta G°$ ($G_{products} - G_{reactants}$) is negative and K is greater than 1. The reaction proceeds spontaneously to the products; that is, it proceeds spontaneously to the lower energy or more stable compound(s). The situation is reversed in part (b) of the figure. The reactants are more stable, $\Delta G°$ is positive, K is less than 1, and the reactants are favored at equilibrium.

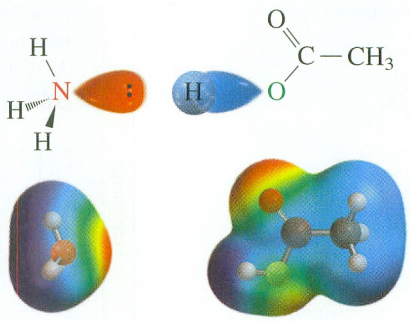
PROBLEM 4.11

Draw diagrams like that in Figure 4.3 for the reactions in problem 4.9.

4.3 RATE OF THE ACID–BASE REACTION

As you should recall from general chemistry, a favorable equilibrium constant is not sufficient to ensure that a reaction will occur. In addition, the rate of the reaction must be fast enough that the reaction occurs in a reasonable period of time. The reaction rate depends on a number of factors. First, the reactants, in this case the acid and the base, must collide. In this collision the molecules must be oriented properly so that the orbitals that will form the new bond can begin to overlap. The orientation required for the orbitals of the reactants is called the **stereoelectronic requirement** of the reaction. (*Stereo* means dealing with the three dimensions of space.) In the acid–base reaction, the collision must occur so that the atomic orbital of the base that is occupied by the unshared pair of electrons can begin to overlap with the 1*s* orbital of the acidic hydrogen.

In the case of the reaction of ammonia with acetic acid, the stereoelectronic requirement can be pictured as follows:



If, instead, the collision were to occur so that the orbital on the nitrogen bumped into some other part of the acetic acid molecule, that collision would not lead to an acid–base reaction.

You might also recall that an energy barrier separates the reactants and the products in most reactions. Therefore, a final requirement for a collision to lead to reaction is that the collision must provide enough energy to surmount this energy barrier. This extra energy is called the **activation energy** for the reaction. Activation energy will be considered in more detail when more complicated reactions are discussed. For now, it is enough to note that the activation energy for acid–base reactions is usually small.

A diagram that shows how the free energy of the system changes as a reaction proceeds is often very informative. Such a diagram has the free energy, G, on the y-axis, just as in Figure 4.3, but has a measure of the progress of the reaction along the x-axis, so the reactants are shown on the left-hand side of the diagram and the products on the right-hand side. Figure 4.4 shows such a diagram for the ionization of HBr in water. Because HBr is a strong acid, $\Delta G°$ for this reaction is negative and $K_a > 1$. The products are favored at equilibrium because they are more stable than the reactants. The line connecting the energy of the reactants to that of the products shows how the energy changes during the reaction. As the reaction proceeds, there is initially a slight increase

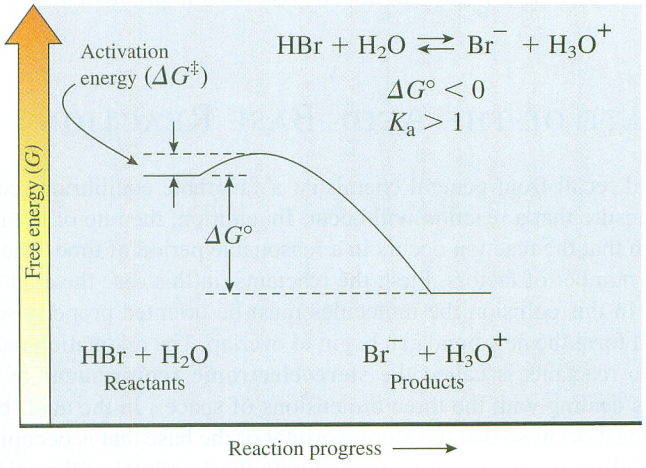


Figure 4.4

FREE ENERGY VERSUS REACTION PROGRESS DIAGRAM FOR THE REACTION OF HBr WITH H_2O.

in energy, followed by a decrease as the reaction proceeds toward the products. The size of the energy barrier that the reaction must pass over is called the activation energy, $\Delta G^{\ddagger}$. In this case, $\Delta G^{\ddagger}$ is very small, so the energy barrier is easily overcome—the reaction is very fast. These energy versus reaction progress diagrams are very useful and will be encountered often in subsequent chapters.

A **mechanism** for a reaction shows the individual steps in the reaction. It shows how the nuclei and electrons move as the reaction proceeds, how the bonds change, and the order in which the bonds are made and broken. The acid–base reaction has a very simple mechanism. It consists of only one step, which involves breaking the bond between the acid and the hydrogen and forming the new bond between the base and the hydrogen. The free energy versus reaction progress diagram has only a single energy barrier between the reactants and the products. Mechanisms for more complicated organic reactions may involve several different steps in which different bonds are made or broken. Each step has an energy barrier that separates the reactant and product of that step. Reaction mechanisms are very important. Understanding the mechanism for a more complicated reaction will enable us to predict and remember many features of the reaction, such as how to increase the rate, how to maximize the amount of product that is formed, and so forth.

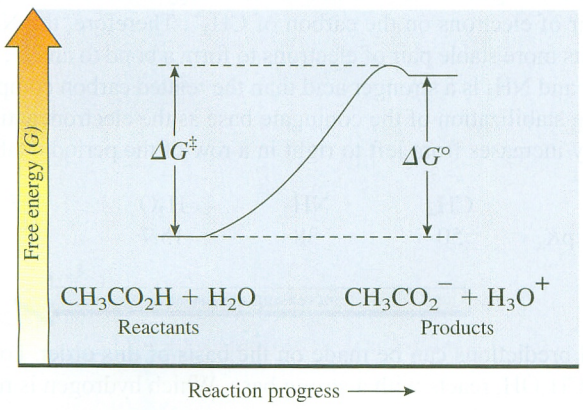
Because the activation energies are small and the stereoelectronic requirements are not difficult to meet, most acid–base reactions are very fast in comparison to other types of organic reactions. Therefore, it is usually not necessary to be concerned with the rates of acid–base reactions. In organic reactions that have mechanisms involving several steps, including an acid–base step, one of the other steps in the mechanism usually controls the rate.

PRACTICE PROBLEM 4.4

Show a free energy versus reaction progress diagram for this reaction.

Solution

First we must determine whether the reactants or the products are more stable. Acetic acid is a weak acid (see Figure 4.2), so the equilibrium favors the reactants. In other words, $K_a < 1$ and $\Delta G^{\circ} > 0$. The diagram is just the reverse of that shown in Figure 4.4.



Note that the magnitude of the activation energy, $\Delta G^{\ddagger}$, is slightly larger than that of $\Delta G°$ in this case. This means that there is only a small activation barrier for the reverse reaction.

PROBLEM 4.12

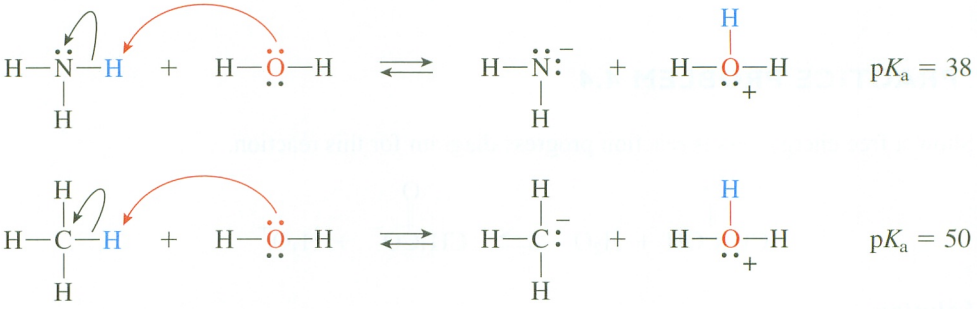
Show a free energy versus reaction progress diagram for the following reaction:

$$HCl + NH_3 \rightleftharpoons Cl^- + {}^+NH_4$$

4.4 Effect of the Atom Bonded to the Hydrogen on Acidity

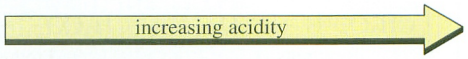
It is important to understand the various factors that determine the strength of an acid—that is, why one compound is a stronger acid than another. Such an understanding makes it much easier to remember whether a particular compound is a strong acid or a weak acid. In addition, it then becomes possible to make qualitative predictions about what a change in the structure of a compound will do to its K_a value. Therefore, most of the remainder of this chapter is a discussion of how the structure of the acid affects its strength. The effects to be discussed are the atom to which the hydrogen is bonded, nearby charges or polar bonds, hydrogen bonding, the hybridization of the atom to which the hydrogen is bonded, and resonance. First, let's consider the effect of the atom bonded to the acidic hydrogen.

Consider the following acid–base reactions:



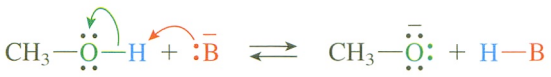
The hydrogen that is bonded to carbon is 10^{12} times less acidic than the hydrogen that is bonded to nitrogen. This can be explained by considering the electronegativities of the carbon and the nitrogen. Nitrogen is more electronegative than carbon. The unshared pair of electrons on the nitrogen of NH_2^- is in a lower-energy orbital, and is more stable, than the unshared pair of electrons on the carbon of CH_3^-. Therefore, the NH_2^- has less inclination to use its more stable pair of electrons to form a bond to an H^+, so it is a weaker base than CH_3^-, and NH_3 is a stronger acid than the related carbon compounds. Because of this increasing stabilization of the conjugate base as the electronegativity of the atom increases, acidity increases from left to right in a row of the periodic table.

	CH_4	NH_3	H_2O	HF
pK_a	50	38	15.7	3



Many useful predictions can be made on the basis of this order. For example, suppose methanol, CH_3OH, reacts with a strong base. Which hydrogen is removed? Which

hydrogen is more acidic? Because oxygen is more electronegative than carbon, the hydrogen on the oxygen is considerably more acidic than the hydrogens on the carbon. The reaction that occurs is

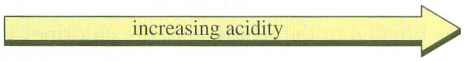


In general, oxygen acids (H bonded to O) will be stronger than carbon acids (H bonded to C), other things being equal.

When comparisons are made within a column of the periodic table, it is found that electronegativity is no longer the controlling factor. Acidity increases from top to bottom in a column of the periodic table, whereas electronegativity decreases.

	HF	HCl	HBr	HI
pK_a	3	−7	−9	−10

		H_2O	H_2S	
pK_a		15.7	7	



Part of the explanation for this trend is that atoms that are lower in a column form weaker bonds to hydrogen because their larger atomic orbitals do not overlap as well with the small hydrogen 1*s* orbital. These weaker bonds make removing the proton easier. The ability of larger anions to better accommodate a negative charge also contributes to this trend.

PROBLEM 4.13

Which species is a stronger acid?

a) H_2S or HCl **b)** PH_4^+ or NH_4^+ **c)** CH_3CH_3 or H_2S

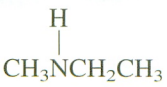
PROBLEM 4.14

Which anion is the stronger base?

a) HO^- or HS^- **b)** $CH_3\bar{N}H$ or $CH_3\bar{O}$

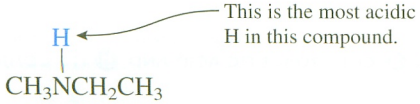
PRACTICE PROBLEM 4.5

Which is the most acidic hydrogen in this compound?



Solution

If none of the other effects described in subsequent sections are operating, a hydrogen on a nitrogen is more acidic than a hydrogen on a carbon because the nitrogen is more electronegative than the carbon.



PROBLEM 4.15

Which is the most acidic hydrogen in each of these compounds?

a) $H_2NCH_2CH_2OH$ **b)** CH_3CH_2OH **c)** CH_3SH

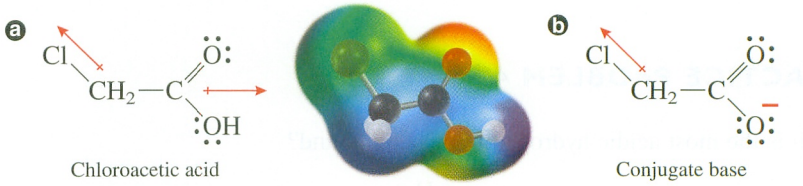
4.5 INDUCTIVE EFFECTS

The effect of a nearby dipole in a molecule on a reaction elsewhere in that molecule is termed an **inductive effect.** Consider two carboxylic acids, acetic acid and chloroacetic acid:

CH_3COOH	$ClCH_2COOH$
Acetic acid	Chloroacetic acid
$pK_a = 4.76$	$pK_a = 2.86$

Replacing one of the hydrogens of acetic acid with a chlorine results in an increase in acid strength by almost a factor of 100. Remember that the acidic hydrogen in these molecules is the one bonded to the oxygen, so the chlorine is actually exerting its effect from several bonds away from the reacting bond. Figure 4.5 shows how the presence of the dipole of the C—Cl bond increases the energy of the acid (a), while it lowers the energy of the conjugate base (b). The inductive effect of the chlorine destabilizes the acid and stabilizes the conjugate base. Figure 4.6 shows how this inductive effect changes $\Delta G°$ for the acid–base reaction of chloroacetic acid as compared to acetic acid. Chloroacetic acid is destabilized relative to acetic acid by the inductive effect of the chlorine. In contrast, the conjugate base of chloroacetic acid is stabilized relative to the conjugate base of acetic acid. Therefore, $\Delta G°_2$ for the acid–base reaction of chloroacetic acid is less than $\Delta G°_1$ for that of acetic acid. The value of K_a is larger for chloroacetic acid—it is a stronger acid than acetic acid.

Organic chemists often talk about the inductive effect of a group. Chlorine is an electron-withdrawing group relative to hydrogen because of its inductive effect; that is,



In chloroacetic acid the interaction of the dipole of the Cl—C bond with the dipole of the carboxylic acid group is destabilizing because the positive end of one dipole is closer to the positive end of the other. The interaction of these like charges is repulsive and increases the energy of the molecule.

In the conjugate base of chloroacetic acid the interaction of the positive end of the Cl—C dipole with the negative charge of the ionized carboxylate group is a stabilizing interaction. The energy of the anion is lowered by this effect.

Figure 4.5

CHARGE INTERACTIONS IN (a) CHLOROACETIC ACID AND (b) ITS CONJUGATE BASE.

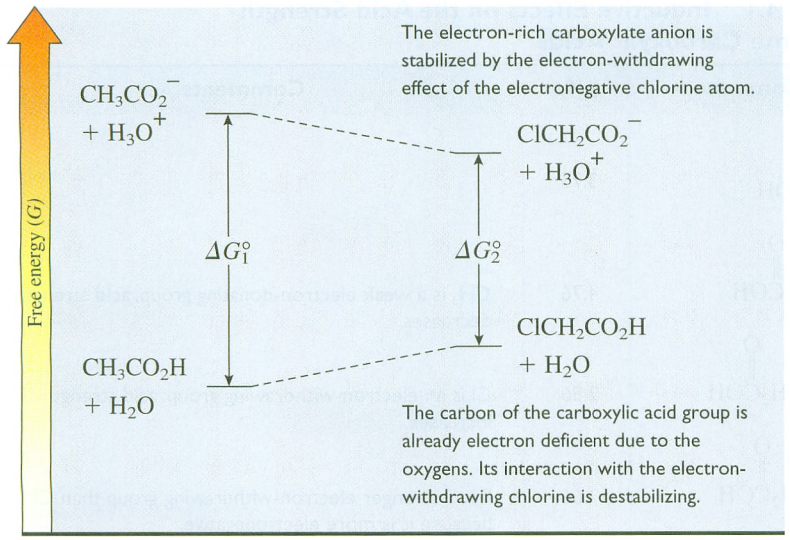
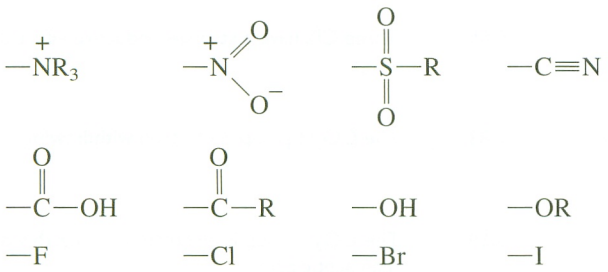

Free energy (G)
$CH_3CO_2^- + H_3O^+$
$ClCH_2CO_2^- + H_3O^+$
ΔG_1°
ΔG_2°
$ClCH_2CO_2H + H_2O$
$CH_3CO_2H + H_2O$
The electron-rich carboxylate anion is stabilized by the electron-withdrawing effect of the electronegative chlorine atom.
The carbon of the carboxylic acid group is already electron deficient due to the oxygens. Its interaction with the electron-withdrawing chlorine is destabilizing.

Figure 4.6

INDUCTIVE EFFECT ON THE FREE-ENERGY CHANGES IN AN ACID–BASE REACTION.

it pulls more electron density away from its bond partner than does hydrogen. Because most functional groups contain atoms that are more electronegative than hydrogen, they are also inductive electron-withdrawing groups. The following is a partial list of inductive electron-withdrawing groups:



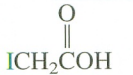
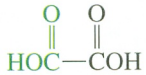
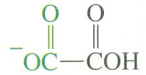
Inductive electron-withdrawing groups

In contrast, only a few groups are electron-donating relative to hydrogen because of their inductive effects. Two of these are electron rich because of their negatively charged oxygen atoms. In addition, alkyl groups, such as CH_3 and CH_2CH_3, behave as weak electron-donating groups in many situations:

Inductive electron-donating groups

Replacing a hydrogen with an electron-withdrawing group will destabilize an electron-poor site or stabilize an electron-rich site. Because the conjugate base is always more electron rich than the acid, replacing a hydrogen with an electron-withdrawing group re-

Table 4.1 Inductive Effects on the Acid Strength of Some Carboxylic Acids

Compound	pK_a	Comments
	3.75	
	4.76	CH_3 is a weak electron-donating group; acid strength decreases.
	2.86	Cl is an electron-withdrawing group; acid strength increases.
	2.66	F is a stronger electron-withdrawing group than Cl because it is more electronegative.
	3.12	I is less electronegative and a weaker electron-withdrawing group than Cl.
	3.98	The Cl is farther from the reaction site; the inductive effect decreases rapidly with increasing distance.
	0.65	Three Cl's have a stronger inductive effect than one.
	2.83	The CO_2H group is electron withdrawing.
	5.69	The CO_2^- group is electron donating; this is a weaker acid than acetic acid.

sults in a stronger acid. Replacing a hydrogen with an electron-donating group has the opposite effect. Table 4.1 provides some examples of inductive effects on the acidities of carboxylic acids.

PROBLEM 4.16

Explain which compound is the stronger acid:

a) CHF_2CO_2H or CH_2FCO_2H

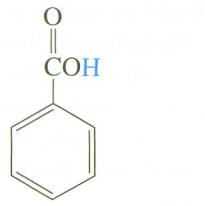
b) CHF_2CO_2H or $CHBr_2CO_2H$

c) $CH_3OCH_2CO_2H$ or CH_3CO_2H

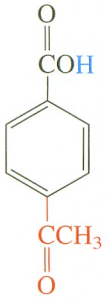
4.6 HYDROGEN BONDING

If the acidic hydrogen forms a hydrogen bond with another atom in the same molecule, the strength of the acid is decreased. It is more difficult for a base to remove the proton because the hydrogen bond must be broken in addition to the regular sigma bond to the hydrogen. However, this effect is complicated by the inductive effect of the group involved in the hydrogen bond (Figure 4.7).

The inductive effect and the hydrogen-bonding effect in *o*-acetylbenzoic acid (see Figure 4.7) are operating in opposite directions. The inductive effect increases the acid strength while the hydrogen bond decreases it. Although the two effects nearly cancel out in this particular case, this cannot usually be predicted in advance. In general, the direction of an effect—that is, whether it is acid strengthening or acid weakening—can readily be determined. However, it is much more difficult to estimate the magnitude of the effect. In a case such as *o*-acetylbenzoic acid, in which the two effects are opposed, it is difficult to predict which one is larger, so it is not possible to predict whether the acid is stronger or weaker than the model compound, in which neither effect is present. Therefore, most of our predictions will be qualitative rather than quantitative—we will be able to determine that one compound is a stronger acid (or reacts faster) than another, but we will not be able to predict exactly how much stronger (or faster).

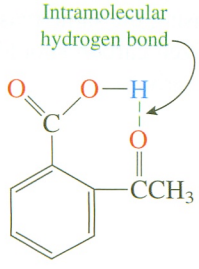


Benzoic acid
$pK_a = 4.19$



p-Acetylbenzoic acid
$pK_a = 3.70$

The $CH_3C{=}O$ group (the acetyl group) is electron withdrawing. When it is substituted on the ring position opposite the carboxylic acid group, its inductive effect increases the strength of this acid as compared to benzoic acid.



o-Acetylbenzoic acid
$pK_a = 4.13$

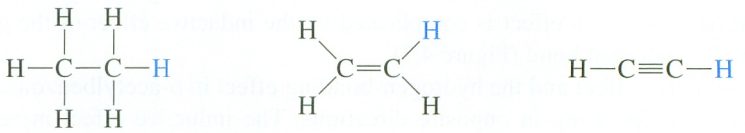
If the acetyl group is substituted on the position adjacent to the carboxylic acid group, an even stronger acid should result because the inductive effect increases as the groups are brought closer together. However, this acid is weaker than the previous example; its pK_a is similar to that of benzoic acid. The acid-strengthening inductive effect is canceled by the acid-weakening effect of the hydrogen bond formed between the hydrogen of the carboxylic acid group and the oxygen of the acetyl group.

Figure 4.7

INDUCTIVE EFFECTS AND HYDROGEN BONDING EFFECTS.

4.7 HYBRIDIZATION

As the following examples show, the hybridization of the atom bonded to the hydrogen has a large effect on the acidity of that hydrogen:



Ethane
$pK_a = 50$

Ethene
$pK_a = 44$

Ethyne
$pK_a = 25$

In this series, as the hybridization changes from sp^3 in ethane to sp^2 in ethene and to sp in ethyne, the acidity increases and the pK_a decreases. This is because of the relative stability of the unshared electrons in the conjugate bases of each of these compounds.

Figure 4.8 shows the energies of the hybrid orbitals relative to the s and p orbitals from which they are formed. An sp hybrid orbital is composed of 50% p orbital and 50% s orbital. Therefore, its energy is halfway between the energies of the s orbital and the p orbital. Similarly, the energy of an sp^2 orbital is higher than that of the s orbital by 67% of the difference between the energies of the p orbital and the s orbital, and the energy of an sp^3 orbital is higher than the energy of the s orbital by 75% of this difference.

The unshared pair of electrons of the conjugate base of ethane occupies an sp^3 atomic orbital on the carbon. The unshared pair of electrons of the conjugate base of ethene occupies an sp^2 atomic orbital. Because the sp^2 orbital is lower in energy, the unshared electrons in this orbital in the conjugate base of ethene are more stable (and less basic) than the electrons in the sp^3 orbital of the conjugate base of ethane. Thus, ethene is a stronger acid than ethane. Because the electrons of the conjugate base of ethyne are even lower in energy in an sp orbital, ethyne is an even stronger acid.

This explanation using orbital energies can also be couched in terms of electronegativities. Electronegativity and orbital energy are directly related. For example, the reason why fluorine is more electronegative than oxygen is that the $2p$ orbital of fluorine is lower in energy than the $2p$ orbital of oxygen. Because an added electron would prefer to occupy the lower-energy orbital, fluorine is more electronegative. An sp orbital is lower in energy than an sp^2 orbital, so it might be said that an sp-hybridized carbon is more electronegative than an sp^2-hybridized carbon. Therefore, using the same reasoning as in Section 4.4, a hydrogen that is bonded to an sp-hybridized carbon should be more acidic than a hydrogen that is bonded to an sp^2-hybridized carbon.

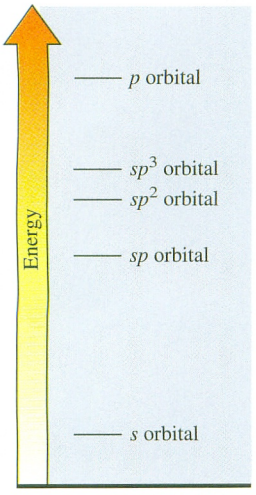


Figure 4.8

ENERGIES OF HYBRID ATOMIC ORBITALS RELATIVE TO *s* AND *p* ATOMIC ORBITALS.

PROBLEM 4.17

Which is the most acidic hydrogen in $CH_3CH_2C{\equiv}CH$?

4.8 RESONANCE

Stabilization by resonance is used to explain many observations in organic chemistry. Resonance stabilization of a product can shift an equilibrium dramatically to the right, that is, to the product side of the reaction. Resonance can also lower the activation energy for a reaction, resulting in a considerable increase in reaction rate. What we learn

Focus On

Calcium Carbide

Because of its *sp* hybridization, ethyne is a strong enough acid that its conjugate base can be readily generated by using one of the strong bases that are available in the laboratory. Calcium carbide, CaC_2, a relatively stable solid, can be viewed as a dianion of ethyne:

$$Ca^{2+}\ {}^{-}:C{\equiv}C:^{-}$$

Calcium carbide

Calcium carbide is prepared by the reaction of calcium oxide with carbon, in the form of coke, at very high temperatures:

$$CaO + 3\,C \xrightleftharpoons{2000\text{–}3000^\circ C} CaC_2 + CO$$

As expected, the carbide dianion is a very strong base and readily removes protons from water to produce ethyne (acetylene) gas:

$$Ca^{2+}\ {}^{-}:C{\equiv}C:^{-} + 2\,H{-}OH \longrightarrow H{-}C{\equiv}C{-}H + Ca(OH)_2$$

Calcium carbide provides a fairly safe and easy-to-handle source of ethyne. Before the advent of battery-operated lights, portable lamps such as those used on bicycles, carriages, and miner's helmets were fueled by this material. Water was slowly dropped onto solid calcium carbide, and the ethyne that was generated was burned. This reaction is still used as a source of acetylene for welding torches.

Ethyne can be used as a starting material for the preparation of many industrially important organic compounds. Currently, it is more cost-effective to prepare these compounds from petroleum. However, as petroleum supplies dwindle in the future, ethyne prepared from coal via calcium carbide will become more economically attractive as a source of these compounds.

here about how resonance affects the acid–base equilibrium will be very useful in discussions of both equilibria and rates of other reactions in subsequent chapters.

Consider the acid–base reactions of ethanol and acetic acid in water:

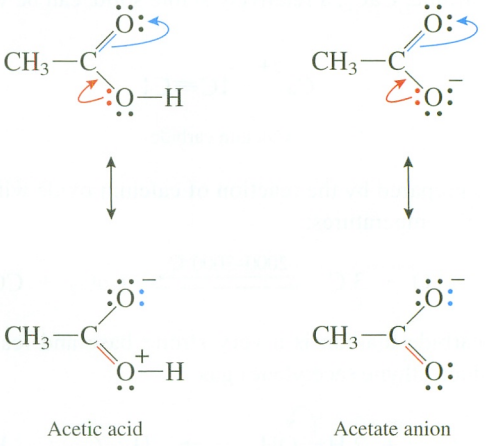
$$CH_3CH_2OH + H_2O \rightleftharpoons CH_3CH_2O^- + H_3O^+ \qquad pK_a = 16$$

Ethoxide ion

$$CH_3\overset{\displaystyle O}{\overset{\|}{C}}OH + H_2O \rightleftharpoons CH_3\overset{\displaystyle O}{\overset{\|}{C}}O^- + H_3O^+ \qquad pK_a = 4.76$$

Acetic acid is a stronger acid than ethanol by a factor of about 10^{11}. In both compounds the acidic hydrogen is bonded to an oxygen. Replacing the CH_2 of ethanol with a C=O results in an enormous increase in acidity. Part of this increase is due to the inductive effect of the oxygen of the carbonyl group, but the effect is much too large to be due only to this.

The other factor that is contributing to the dramatic increase in the acidity of acetic acid is resonance stabilization. Neither ethanol nor its conjugate base, which is called ethoxide ion, is stabilized by resonance. The following resonance structures can be written for acetic acid and its conjugate base, acetate anion:

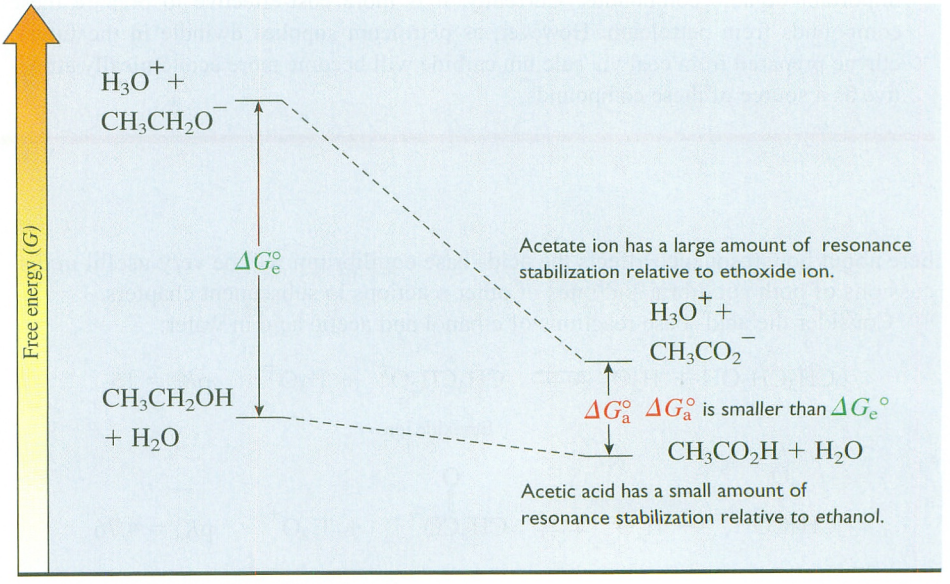


As noted in Figure 3.16, acetic acid has only a small amount of resonance stabilization because the lower structure is only a minor contributor to the resonance hybrid. Acetate ion has a large amount of resonance stabilization because it has two equivalent contributors to the hybrid.

Figure 4.9 diagrams these energy changes. Because acetic acid has only a small amount of resonance stabilization, its energy is lowered only a little as compared to

Figure 4.9

ENERGY DIAGRAM FOR THE REACTION OF ETHANOL AND ACETIC ACID AS ACIDS IN WATER.



ethanol. However, acetate ion has a much larger amount of resonance stabilization so its energy is lowered more relative to ethoxide ion. Therefore, $\Delta G°_a$ is smaller than $\Delta G°_e$, resulting in acetic acid being a stronger acid than ethanol.

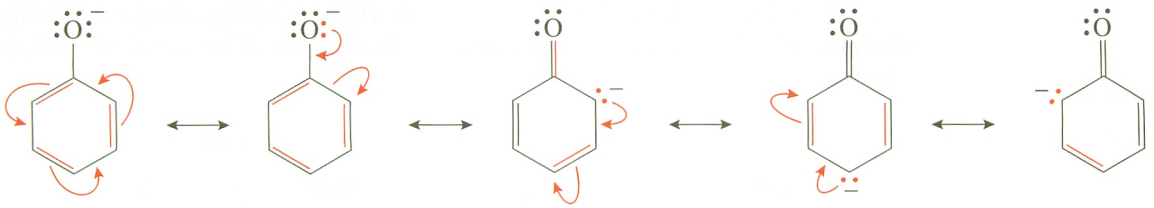
In other words, the unshared electron pair of the base, acetate ion, is delocalized (spread over both oxygens) by resonance. This electron pair is stabilized and less available for bonding to the proton, which localizes this electron pair in the sigma bond and costs resonance energy. The most common effect of resonance on an acid–base reaction is to delocalize and stabilize the unshared electron pair of the conjugate base, resulting in a stronger acid.

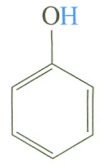
To make this more clear, consider the following examples. Replacing one H of water with a CH_3CH_2 group to give ethanol should have only a small effect on acidity, so ethanol (and other alcohols) are expected to have pK_a's close to that of water. The pK_a of ethanol is about 16; the pK_a of water is 15.74.

CH_3CH_2OH

Ethanol
pK_a = 16

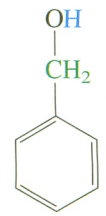
Phenol resembles an alcohol, but with the OH attached to an aromatic ring rather than an alkyl group. However, its pK_a is 10. It is a stronger acid than ethanol by a factor of 10^6. The aromatic ring has caused a large increase in acidity. Five important resonance structures can be written for the conjugate base of phenol. One of them is the benzene resonance structure that is present in all aromatic compounds and does not affect the basicity because it stabilizes both the acid and the conjugate base equally. The others delocalize one unshared electron pair of the basic oxygen, stabilizing the base and making it weaker. (Although similar resonance structures can be written for phenol itself, they are less important because they have formal charges.) Furthermore, note that the delocalized pair of electrons occupies alternating positions around the ring in the various resonance structures. Both of these observations will be useful in subsequent discussions. The last three resonance structures are not as important as the first two because the negative charge is on a carbon rather than the more electronegative oxygen. Therefore, the overall amount of resonance stabilization is not as large as in the case of acetate, which has two equivalent resonance contributors. Phenol is a weaker acid than acetic acid.





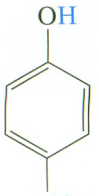
Phenol
pK_a = 10

At first glance, benzyl alcohol resembles phenol and it might be expected to have a pK_a near 10. However, its pK_a is actually close to 16; it resembles ethanol more than phenol in acid strength. The CH_2 group between the OH and the aromatic ring prevents any resonance interaction between the electrons on the oxygen and the ring—the CH_2 acts something like an insulator. In other words, the electrons on the oxygen are not conjugated with the double bonds of the ring because of the CH_2 group. Remember that resonance does not usually affect acid strength unless it involves the unshared electrons of the conjugate base. Resonance that stabilizes both the acid and the conjugate base equally, as in this case, has no effect on acidity.



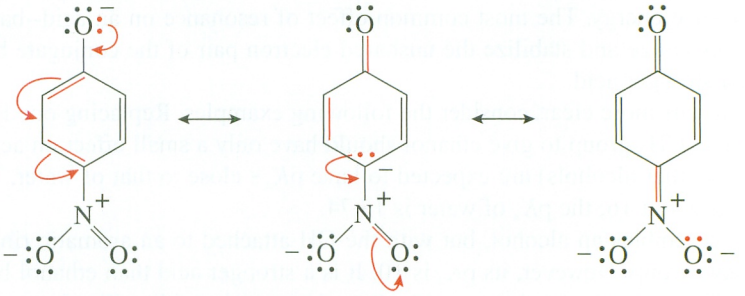
Benzyl alcohol
pK_a = 16

The pK_a of *p*-nitrophenol is 7.15; it is a stronger acid than phenol by a factor of 700. This is due in part to the electron-withdrawing inductive effect of the nitro



p-Nitrophenol
$pK_a = 7.15$

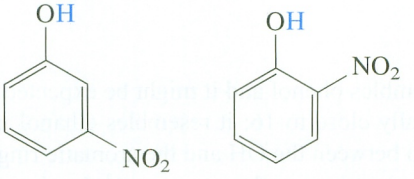
group. However, the nitro group also provides additional delocalization of the unshared electrons of the conjugate base. When the electrons are placed on the carbon bonded to the nitro group, they can be delocalized onto the oxygen of the nitro group. This extra resonance stabilization is the principal reason for the increase in acidity for this compound.



The pK_a of *m*-nitrophenol is 8.36. The nitro group is not nearly as effective in increasing acidity when it is substituted on this position of the ring as in the case of *p*-nitrophenol, even though its inductive effect should be stronger because it is closer to the OH. The reason for this is the absence of a resonance structure where the electrons are delocalized onto the nitro group in this isomer. Examination of the resonance structures of the conjugate base shows that the electron pair is never on the carbon to which the nitro group is attached, so it cannot be delocalized onto the oxygen of the nitro goup. (Remember that the electron pair is delocalized onto alternating positions.) The nitro group exerts only an inductive effect.

o-Nitrophenol has the OH and NO_2 groups bonded to adjacent carbons. Its pK_a is 7.22. This isomer has the same type of resonance stabilization as *p*-nitrophenol. The inductive effect of the nitro group is stronger because it is closer to the OH (acid strengthening) and the acidic hydrogen is hydrogen bonded to the oxygen of the nitro group (acid weakening). These latter two effects nearly cancel in this case.

Picric acid is a strong acid with a pK_a of 0.42. The acid-strengthening effect of the three nitro groups, which all can delocalize the electron pair of the conjugate base, is quite large.



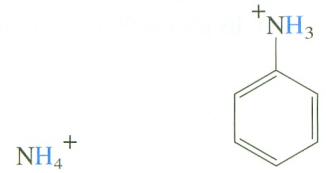
m-Nitrophenol
$pK_a = 8.36$

o-Nitrophenol
$pK_a = 7.22$

2,4,6-Trinitrophenol
(picric acid)
$pK_a = 0.42$

Ammonium ion is a weak acid. Its pK_a is 9.24. On the basis of arguments similar to those presented earlier for phenol, the conjugate acid of aniline is expected to be a

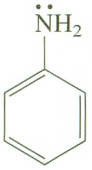
stronger acid than ammonium ion because of resonance stabilization of its conjugate base. It is a stronger acid by a factor of more than 10^4; its pKa is 4.63.



$pK_a = 9.24$

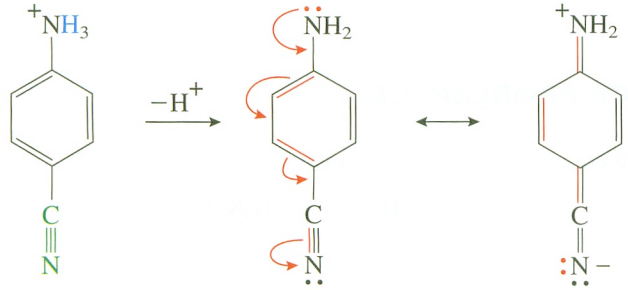
Conjugate acid of aniline
$pK_a = 4.63$

Which is the stronger base, aniline or ammonia? The same reasoning applies. Aniline is stabilized by resonance. The basic pair of electrons is delocalized into the ring and is less available to form a covalent bond, so it is a weaker base. (Of course, if the conjugate acid of aniline is stronger than ammonium ion, then aniline must be a weaker base than ammonia.)



Aniline

The cyano group of *p*-cyanoaniline exerts an electron-withdrawing inductive effect and can delocalize the electron pair of the base by resonance. On the basis of reasoning identical to that presented for *p*-nitrophenol, the conjugate acid of *p*-cyanoaniline should be a stronger acid than the conjugate acid of aniline. Indeed, this is the case; the pK_a is 1.74.



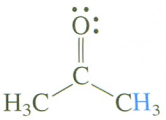
$pK_a = 1.74$

p-Cyanoaniline

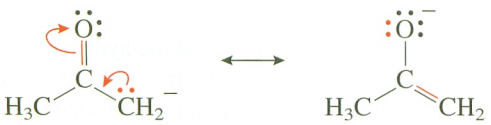
Alkanes like ethane, with pK_a's around 50, are the weakest acids commonly encountered in organic chemistry. Their conjugate bases are much too strong to be generated by the methods that are used to make other, less strong bases. The pK_a for acetone is 20. The C=O has increased the acidity of the hydrogen on the adjacent C by a factor of 10^{30} compared to ethane. In this case the electrons of the conjugate base are delocalized onto an electronegative oxygen atom, resulting in an enormous increase in acidity. (Note the similarity to the case of acetic acid.) Anions similar to this one are very important in organic chemistry and can be readily generated by treating the conjugate acid with one of the very strong bases that are available in the laboratory. They are encountered often as important reagents or as intermediates in reactions.

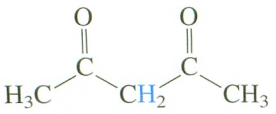
CH_3CH_3

Ethane
$pK_a = 50$



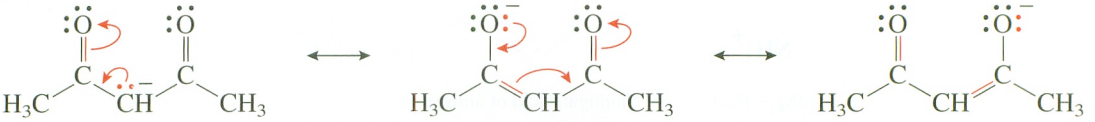
Acetone
$pK_a = 20$





2,4-Pentanedione
$pK_a = 9$

The most acidic hydrogen of 2,4-pentanedione is on the carbon between the two C=O groups. If this hydrogen is removed, the new unshared electron pair of the conjugate base is delocalized onto both of the oxygens. The additional resonance stabilization causes this compound to be an even stronger acid. Its pKa is 9; it is a stronger acid than water.



These examples illustrate the importance of looking for resonance stabilization in predicting the strength of an acid. Remember that resonance usually stabilizes the conjugate base more than the acid. To do this and to be effective in increasing the acidity, resonance must involve the newly generated unshared pair of electrons of the conjugate base, delocalizing them so that they are less available for bonding to the proton. This makes the conjugate base weaker, and hence the acid is stronger.

PROBLEM 4.18

Show the resonance structures for the conjugate base of the meta isomer of nitrophenol and confirm that the nitro group is less effective at stabilizing this anion than it is in the case of the para isomer.

PRACTICE PROBLEM 4.6

Explain which compound is a stronger acid:

$$CH_3CH_3 \text{ or } CH_3NO_2$$

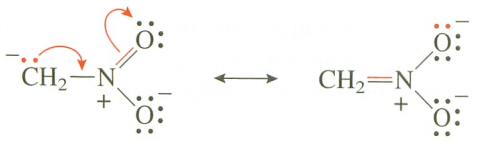
Strategy

First identify the acidic hydrogen in each compound. Then draw the conjugate base that is formed when this hydrogen is removed. Remember the five factors that can affect the strength of the acid: (1) the atom to which the hydrogen is bonded, (2) an inductive effect, (3) hydrogen bonding involving the acidic hydrogen, (4) the hybridization of the atom to which the hydrogen is bonded, and (5) a resonance effect. Determine which effect is operative in the case being considered. Is the atom to which the hydrogen is bonded different in the compounds being compared (factor 1)? Is there a nearby polar bond that can affect the acidity by its inductive effect (factor 2)? Is the hydrogen near an electronegative atom to which it can hydrogen bond (factor 3)? Is the hybridization of the atom to which the hydrogen is bonded different (factor 4)? Or is the electron pair generated in forming the conjugate base part of a conjugated pi system (factor 5)? Then determine which acid or which conjugate base is stabilized by the effect.

Solution

Each compound has only one type of hydrogen, so the hydrogen that is removed to form the conjugate base is easy to identify. The electron pair of the conjugate base from CH_3NO_2 is adjacent to the NO pi bond, so it can be stabilized by resonance. Because

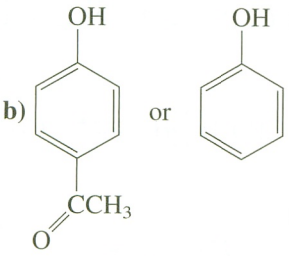
the conjugate base of CH_3CH_3 has no such resonance stabilization, CH_3NO_2 is a stronger acid.

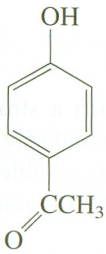
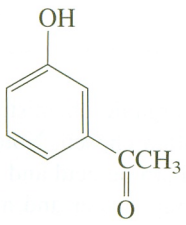


PROBLEM 4.19

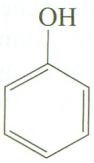
Explain which compound is a stronger acid:

a) $CH_3\overset{\overset{O}{\|}}{C}CH_3$ or $CH_3\overset{\overset{O}{\|}}{C}CH_2C{\equiv}N$

b)  or

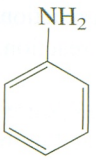
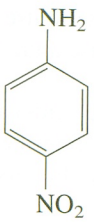
c)  or 

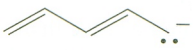
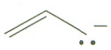
d) CH_3CH_3 or $CH_3\overset{\overset{O}{\|}}{C}OCH_3$

e)  or

PROBLEM 4.20

Explain which compound is the weaker base.

a)  or 

b)  or 

4.9 TABLES OF ACIDS AND BASES

Table 4.2 lists the pK_a values for a number of acids, some inorganic and some organic. Examples of many of the common functional groups are also provided. By using Table 4.2 and the reasoning presented in Sections 4.4 through 4.8, it is possible to make good estimates of the acid strengths of most organic compounds.

PROBLEM 4.21

Use Table 4.2 to predict whether the equilibrium for these reactions favors the reactants or the products.

a) $:\ddot{N}H_2 + CH_3\overset{O}{\overset{\|}{C}}CH_3 \rightleftharpoons \ddot{N}H_3 + \ddot{C}H_2\overset{O}{\overset{\|}{C}}CH_3$

b) $CH_3\overset{O}{\overset{\|}{S}}\ddot{C}H_2 + CH_3CH_2\ddot{O}H \rightleftharpoons CH_3\overset{O}{\overset{\|}{S}}CH_3 + CH_3CH_2\ddot{O}:^-$

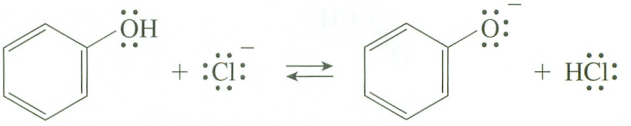
c) 

Table 4.3 lists some common acids used in organic chemistry. When a strong acid is needed, sulfuric or hydrochloric acid is often chosen. Note the similarity of *p*-toluenesulfonic acid to sulfuric acid. It is also a strong acid and is more soluble in organic solvents because of its large organic group. Water and alcohols are acidic enough to react with many strong organic bases.

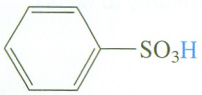
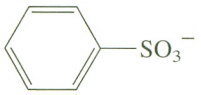
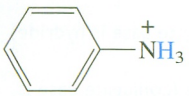
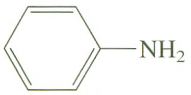
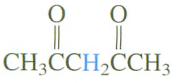
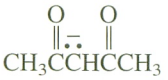
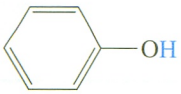
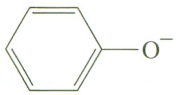
Table 4.4 lists some common bases used in organic chemistry. Although butyllithium behaves as a very strong base in many reactions, it also exhibits other chemistry, so it is usually used to prepare other strong bases listed in the table. Lithium diisopropylamide, sodium amide, dimsyl anion, and sodium hydride are often used to prepare the conjugate bases of aldehydes, ketones, and esters for use in reactions. Potassium *tert*-butoxide is employed when a base somewhat stronger than the conjugate bases of most alcohols is needed.

Sodium hydroxide and sodium ethoxide are used in many reactions where a moderate base will suffice. Carbonate and bicarbonate are often employed to remove acids in the workup of organic reactions. For many of these bases it does not usually matter whether the cation is sodium or potassium.

Some care must be given to the choice of an acid or a base to use in a reaction. It must be strong enough to do the job but not so strong as to cause undesired reactions at other, less reactive functional groups.

Finally, remember that pK_a's more negative than -2 (strong acids) and pK_a's greater than 16 (very weak acids) can be measured only indirectly, so the values listed in these tables are only approximate. For this reason, different sources often list somewhat different values for these acidity constants.

Table 4.2 Approximate Acidity Constants for Some Selected Compounds

Acid	Conjugate Base	pK_a	Name
FSO_3H	FSO_3^-	<-12	Fluorosulfonic acid (a "super acid")
$HClO_4$	ClO_4^-	-10	Perchloric acid
HI	I^-	-10	Hydroiodic acid
H_2SO_4	HSO_4^-	-10	Sulfuric acid
HBr	Br^-	-9	Hydrobromic acid
HCl	Cl^-	-7	Hydrochloric acid
		-6.5	Benzenesulfonic acid (note similarity to sulfuric acid)
ROH_2^+	ROH	-2	Conjugate acid of an alcohol (note similarity to H_3O^+)
H_3O^+	H_2O	-1.74	Conjugate acid of water (hydronium ion)
HNO_3	NO_3^-	-1.4	Nitric acid
HF	F^-	3.17	Hydrofluoric acid
		4–5	Carboxylic acids
		4.63	Conjugate acid of aniline
		6.35	Carbonic acid
		9	2,4-Pentanedione
NH_4^+	NH_3	9.24	Ammonium ion
$HC{\equiv}N$	$^-C{\equiv}N$	9.31	Hydrogen cyanide
RNH_3^+	RNH_2	10–11	Conjugate acid of amines
		10	Phenol
RCH_2NO_2	$R\ddot{C}HNO_2$	10	Nitroalkanes

Continued

Table 4.2 Approximate Acidity Constants for Some Selected Compounds—cont'd

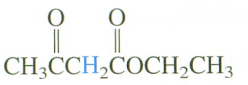
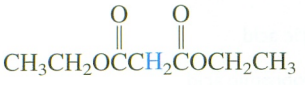
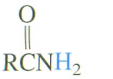
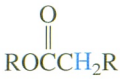
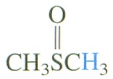
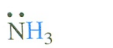
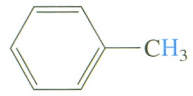
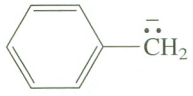
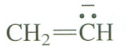
Acid	Conjugate Base	pK_a	Name
		11	Ethyl acetoacetate
		11	Diethyl malonate
H_2O	HO^-	15.74	Water
RCH_2OH	RCH_2O^-	16	Alcohols (note similarity to water)
		17	Amides
		20	Ketones
		25	Esters
$RCH_2{-}CN$		25	Nitriles
$RC{\equiv}CH$	$RC{\equiv}C:^-$	25	Alkynes
H_2	$H:^-$	35	Hydrogen (conjugate base is hydride)
		38	Dimethylsulfoxide (conjugate base is dimsyl ion)
		38	Ammonia (conjugate base is amide ion)
		41	Toluene
$CH_2{=}CH{-}CH_3$		43	Propene
$CH_2{=}CH_2$		44	Ethene
CH_3CH_3		50	Ethane

Table 4.3 Common Acids Used in Organic Chemistry

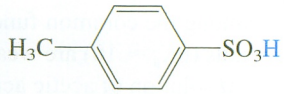
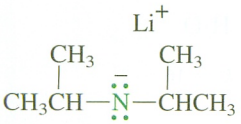
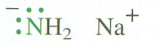
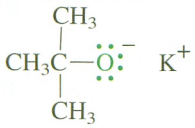
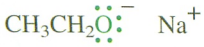
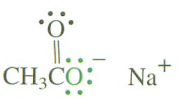
Acid	pK_a	Name
H_2SO_4	−10	Sulfuric acid
HCl	−7	Hydrochloric acid
	−7	*p*-Toluenesulfonic acid
CH_3CO_2H	4.8	Acetic acid
H_2O	15.7	Water
CH_3OH or CH_3CH_2OH	16	Methanol or ethanol

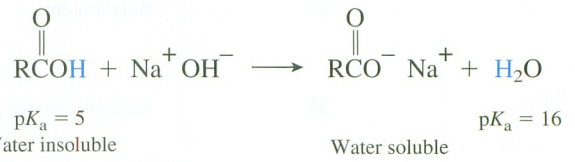
Table 4.4 Common Bases Used in Organic Chemistry

Base	pK_a of Conjugate Acid	Name
$CH_3CH_2CH_2CH_2Li$	50	Butyllithium
	38	Lithium diisopropylamide (LDA)
	38	Sodium amide
	38	Dimsyl anion (conjugate base of dimethyl sulfoxide)
	35	Sodium hydride
	19	Potassium *tert*-butoxide
	16	Sodium ethoxide
	15.7	Sodium hydroxide
CO_3^{2-} 2 Na^+	10.3	Sodium carbonate
$HCO3^-$ Na^+	6.4	Sodium bicarbonate
	4.8	Sodium acetate

4.10 Acidity and Basicity of Functional Groups and Solvents

As can be seen from Table 4.2, most functional groups are only weak acids and/or weak bases. They are too weak to behave as acids or bases in aqueous solution and therefore are said to be neutral. There are three exceptions to this rule among the common functional groups. Carboxylic acids ($pK_a \approx 5$) and substituted phenols ($pK_a \approx 10$) are weak acids. Amines, like ammonia, are weak bases. The pH of a 0.1 *M* solution of acetic acid (CH_3CO_2H) is about 3. Phenol is a weaker acid and the pH of a 0.1 *M* solution is about 5.5. And the pH of a 0.1 *M* solution of CH_3NH_2 is about 11.

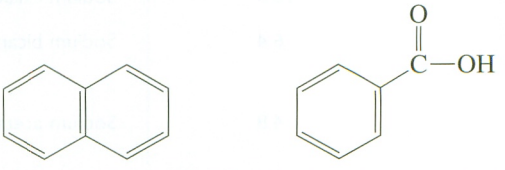
These acidic and basic properties can be used to help identify these functional groups. If an unknown compound is water soluble (has a small R group), then the pH of an aqueous solution of the compound provides an important clue to the functional group that it contains. If the unknown is not soluble in water, its solubility behavior in aqueous acid and base provides the same information. Consider, for example, a carboxylic acid that is not soluble in water. If this acid is added to an aqueous solution of sodium hydroxide, the following reaction occurs:



Hydroxide ion is a strong enough base that the equilibrium for this reaction lies entirely to the right. The insoluble carboxylic acid is converted to its conjugate base, which, as an ionic compound, is quite soluble in water. So the carboxylic acid dissolves (more accurately, it reacts and the product dissolves) in basic solution. Substituted phenols also dissolve in aqueous sodium hydroxide. They can be distinguished from carboxylic acids by using a weaker base. Bicarbonate anion, HCO_3^-, is a strong enough base to react with carboxylic acids but not with phenols. (The pK_a for carbonic acid, H_2CO_3, is 6.35.) So a compound that dissolves in aqueous sodium hydroxide and in aqueous sodium bicarbonate is a carboxylic acid, whereas one that dissolves in aqueous sodium hydroxide but not in aqueous sodium bicarbonate is a phenol.

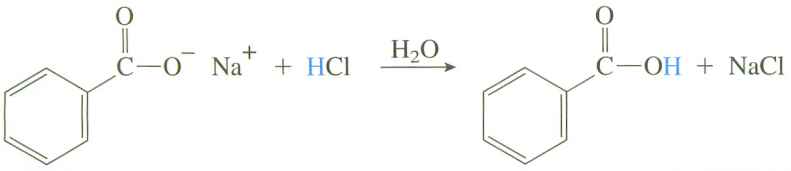
An amine that is insoluble in water reacts with acid to form a salt that dissolves in water, as shown in the following equation. Hydrochloric acid is strong enough that this equilibrium lies entirely toward the product side of the equation.

The acidic or basic properties of these functional groups can also be used to advantage to separate them from neutral compounds. For example, suppose we desire to separate a mixture of naphthalene and benzoic acid:



Naphthalene Benzoic acid

Neither of these compounds is very soluble in water, but both dissolve in a less polar solvent such as dichloromethane (CH_2Cl_2). If this solution is extracted with aqueous sodium hydroxide, the benzoic acid reacts to form a salt that is soluble in the aqueous phase. Therefore, when the two liquids are separated, the carboxylic acid salt is in the aqueous phase and the naphthalene remains in the dichloromethane. The compounds have now been separated. To recover the carboxylic acid, it is necessary to protonate its conjugate base. This can be accomplished by treating the aqueous solution with a strong acid, such as hydrochloric acid. The equilibrium shown in the following equation favors the weaker acid, the carboxylic acid, which then precipitates from the solution:

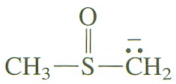


Precipitates

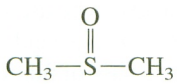
Phenols can be separated from neutral compounds by a similar process. For an amine an acid extraction step followed by making the solution basic is used to accomplish separation from neutral compounds.

When an organic reaction is being designed, the nature of the solvent, especially whether it contains any acidic hydrogens, must be considered. Many of the reagents that are employed in organic reactions are very strong bases. In using such reagents, even weakly acidic solvents must be avoided. For example, suppose we wanted to use sodium amide, $NaNH_2$, in a reaction. This strong base cannot be used in solvents such as ethanol or water because both of these compounds have a weakly acidic hydrogen on the oxygen. An acid–base reaction, such as the one shown in the following equation, would occur, resulting in the destruction of the basic amide anion:

The strongest base that can be used in any particular solvent is the conjugate base of that solvent. Any stronger base will simply react to produce the conjugate base of the solvent. For this reason a base is often used in its conjugate acid as the solvent. For example, NH_2^- is often used in liquid NH_3 as the solvent (NH_3 boils at $-33°C$, so the reaction must be done at low temperature), OH^- is often used in water as the solvent, ethoxide ion ($CH_3CH_2O^-$) is often used in ethanol (CH_3CH_2OH) as the solvent, and the dimsyl anion is often used in DMSO as the solvent:



Dimsyl anion



*Dim*ethyl*sulf*oxide
DMSO

Ethers are also commonly used as solvents for reactions involving strongly basic reagents because they do not have acidic hydrogens but are still polar enough to dissolve the reagents. Ethers that are used include diethyl ether, *tetra*hydro*furan* (THF),

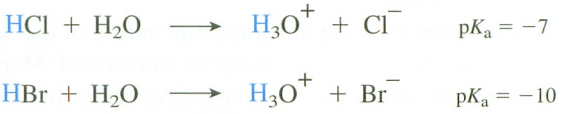
and *dim*ethoxy*e*thane (DME). These compounds are weak enough acids that they can be used with almost any strong base.

PROBLEM 4.22

Explain whether each of the following solvents would be acceptable for reactions involving this anion:

a) Liquid NH_3 **b)** CH_3CH_2OH **c)** $CH_3CH_2OCH_2CH_3$

Just as strong bases react with weakly acidic solvents, strong acids react with even weakly basic solvents. For example, both hydrogen chloride and hydrogen bromide are virtually completely ionized in aqueous solution:



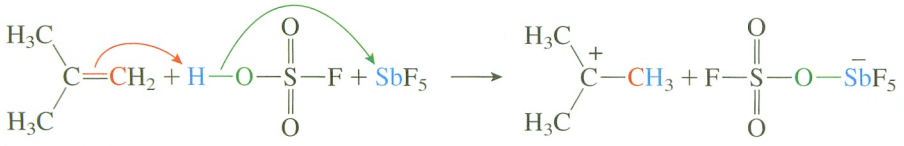
Even though HCl and HBr have different pK_a's, their acid strengths in water are the same because the actual acid that is present in each case is the hydronium ion, H_3O^+. The strongest acid that can be generated in a particular solvent is the conjugate acid of that solvent. Any stronger acid reacts to generate the conjugate acid of the solvent. This is termed the *leveling effect.*

Pure sulfuric acid is a stronger acid than sulfuric acid in water because the acid in aqueous sulfuric acid is actually H_3O^+. Superacids are defined as compounds that are even stronger acids than 100% H_2SO_4. One example of a superacid is fluorosulfonic acid. The inductive effect of the electronegative fluorine makes this a stronger acid than sulfuric acid.

Sulfuric acid Fluorosulfonic acid

Liquid fluorosulfonic acid can be used to protonate extremely weak bases. It can be made even stronger by adding a Lewis acid, such as antimony pentafluoride, SbF_5, which complexes with the conjugate base of fluorosulfonic acid, decreasing its basicity. This mixture, known as magic acid, is so strong that it can protonate extremely weak bases such as the electron pair of a carbon–carbon pi bond as shown in the following equation. (Note that all of the bases we have seen up to this point have had an unshared pair of electrons that are employed to form a bond to the proton of the acid. It takes an extremely strong acid

to protonate the lower-energy electrons in a bonding MO.) The carbocation that is produced is stable enough in a solution of magic acid that its properties can be studied.



Extremely weak base — Lewis acid — A carbocation

George Olah was awarded the 1994 Nobel Prize in chemistry for his work with carbocations and superacids.

Review of Mastery Goals

After completing this chapter, you should be able to:

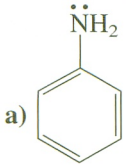
- Write an acid–base reaction for any acid and base. (Problems 4.35 and 4.36)
- Recognize Lewis acids, Lewis bases, and the reactions between them. (Problems 4.25, 4.26, and 4.38)
- Recognize acid or base strengths from K_a or pK_a values and use these to predict the position of an acid–base equilibrium. (Problems 4.23, 4.34, 4.35, 4.36, 4.37, and 4.41)
- Predict and explain the effect of the structure of the compound, such as the atom bonded to the hydrogen, the presence of an electron-donating or electron-withdrawing group, hydrogen bonding, the hybridization of the atom attached to the hydrogen, or resonance, on the strength of an acid or base. (Problems 4.29, 4.30, 4.35, 4.39, 4.40, 4.41, 4.42, 4.43, and 4.47)
- Using the same reasoning, arrange a series of compounds in order of increasing or decreasing acid or base strength. (Problems 4.31, 4.32, and 4.33)
- Identify the most acidic proton in a compound. (Problems 4.24, 4.36, 4.42, and 4.43)

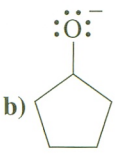
ORGANIC Chemistry Now™
Click *Mastery Goal Quiz* to test how well you have met these goals.

Additional Problems

ORGANIC Chemistry Now™
Assess your understanding of this chapter's topics with additional quizzing and conceptual-based problems at **http://now.brookscole.com/hornback2**

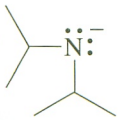
4.23 Show the conjugate acid of each of these species:

a) 

b) 

c) $CH_3CH_2CH_2\ddot{O}H$

d) $CH_3C{\equiv}C:^-$

e) 

4.24 Show the most stable conjugate base of these compounds:

a) CH_3CH_2OH **b)** $HOCCH_2CH_2OH$ **c)** $H_2NCH_2CH_2OH$

4.25 Which of these species can behave as a Lewis acid?

a) $Cl-B(Cl)-Cl$ **b)** $H-C(H)-H$ **c)** $CH_3\overset{+}{C}H_2$

4.26 Which of these species can behave as a Lewis base?

a) $CH_3-\ddot{O}-CH_2CH_3$ **b)** $CH_3CH_2CH_3$ **c)** $CH_3\ddot{N}H_2$

d) $CH_3NH_2^+$ **e)** $CH_3C(=\ddot{O})\ddot{O}H$

4.27 Calculate the pK_a for these compounds.

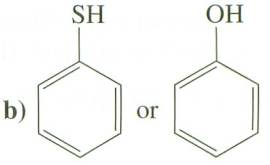
a) $HCOH$ ($K_a = 1.75 \times 10^{-4}$) **b)** CH_3CH_3 ($K_a = 10^{-50}$)

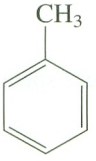
4.28 Calculate the K_a for these compounds:

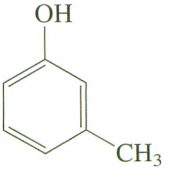
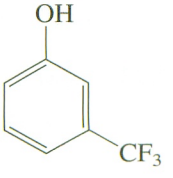
a) $HC{\equiv}CH$ ($pK_a = 25$) **b)** $HC{\equiv}N$ ($pK_a = 9.31$)

4.29 Explain which compound is the stronger acid:

a) CH_3CNH_2 or CH_3COH

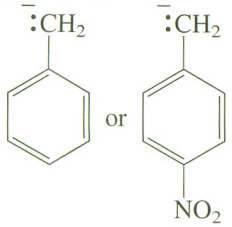
b)  or

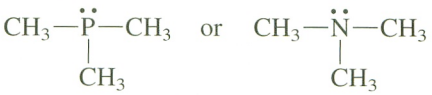
c) $CH_3CH_2CH_2CH_3$ or 

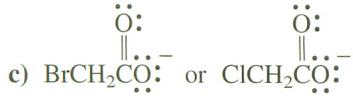
d)  or 

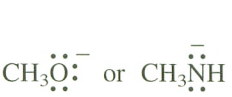
e) CH_3NH_2 or $CH_2{=}NH$

4.30 Explain which species is the stronger base:

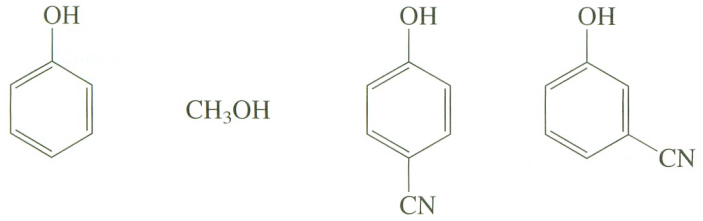
a) 

b) 

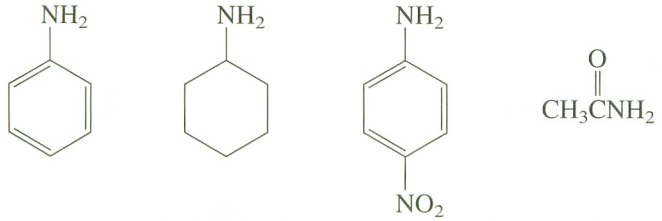
c) 

d) 

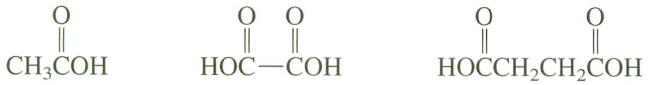
4.31 Arrange these compounds in order of increasing acid strength:



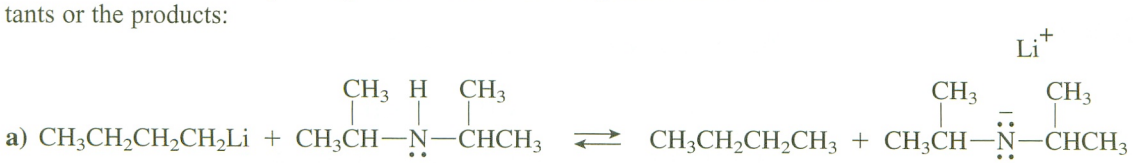
4.32 Arrange these compounds in order of increasing base strength:

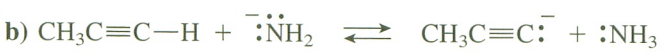


4.33 Arrange these compounds in order of increasing acid strength:



4.34 Use the tables in this chapter to predict whether these equilibria favor the reactants or the products:

a) 

b) 

c)

4.35 Complete these equilibrium reactions in the most reasonable manner possible using the curved arrow convention to show the movement of electrons in the reactions. Predict whether the reactants or the products are favored.

a) $CH_3CH_3 + {}^{-}\!:\!CH_2C{\equiv}N: \rightleftharpoons$

b) $CF_3{-}C(=O){-}O^{-} + CH_3{-}C(=O){-}O{-}H \rightleftharpoons$

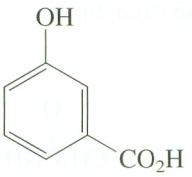
c) $CH_3C(=O){-}NH_2 + CH_3C(=O){-}CH_2^{-} \rightleftharpoons$

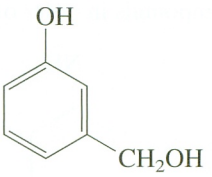
d) $CH_3CH_2CH_2C(=O)OH + {}^{-}OH \rightleftharpoons$

4.36 Identify the most acidic hydrogen in each of these compounds:

a) $HOC(=O)CH_2CH_2S(=O)(=O)OH$

b) $CH_3CH_2CH_2C{\equiv}N$

c) 

d) 

e) $CH_3C(=O)CH_2C(=O)OCH_2CH_3$

f) $H_3\overset{+}{N}CH_2C(=O)OH$

BioLink

4.37 Show the products of these acid–base reactions and predict whether the equilibria favor the reactants or the products:

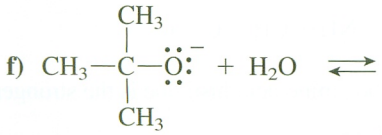
a) $CH_3C(=O)CH_2C(=O)CH_2CH_3 + {}^{-}\!:\!OCH_2CH_3 \rightleftharpoons$

b) $CH_3CH_2NO_2 + CH_3O^{-} \rightleftharpoons$

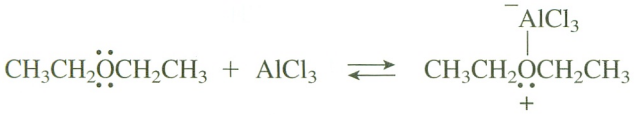
c) $CH_3C(=O)CH_3 + CH_3CH(CH_3){-}\overset{-}{N}{-}CH(CH_3)CH_3 \rightleftharpoons$

d) $FCH_2CH_2{-}C(=O)OH + CH_3CH(F){-}C(=O)O^{-} \rightleftharpoons$

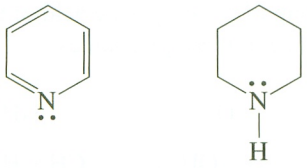
e)

f) 

4.38 Which compound is behaving as the Lewis acid and which as the Lewis base in this reaction?

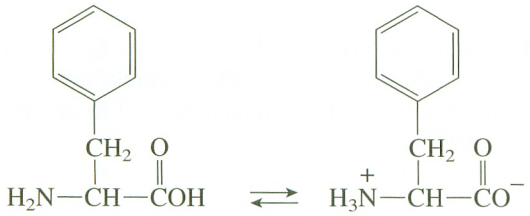


4.39 Explain which of these compounds is the weaker base:



4.40 Explain why the protonation of an amide occurs at the O rather than the N.

4.41 Amino acids contain both a basic functional group, the amine, and an acidic functional group, the carboxylic acid. Thus, they can undergo an internal acid–base reaction as shown in the following equation for the amino acid phenylalanine:

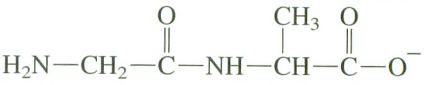


Phenylalanine

Using Table 4.2 and neglecting the effect of one group on the acidity of the other, predict the position of this equilibrium in the case of phenylalanine. Explain whether your prediction is in accord with the experimental observations that phenylalanine melts at 273–276°C and is very soluble in water.

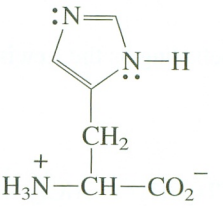
BioLink

4.42 Dipeptides result from the reaction of two amino acids to form an amide. Explain which nitrogen of the following dipeptide is the stronger base:



BioLink

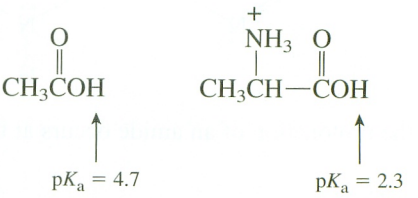
4.43 Explain which nitrogen in the ring of the amino acid histidine is the stronger base:



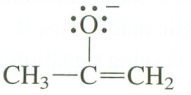
Histidine

BioLink

4.44 The pK_a of the carboxylic acid group of acetic acid is 4.7. The pK_a of the carboxylic acid group of the conjugate acid of the amino acid alanine is 2.3. Explain the difference in these pK_a values.



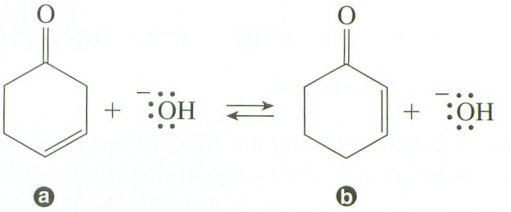
4.45 There are two isomeric conjugate acids that produce the following base. Show the structure of each and explain how they produce the same base upon loss of a proton.



4.46 When ⓐ is reacted with hydroxide ion, isomer ⓑ is formed.

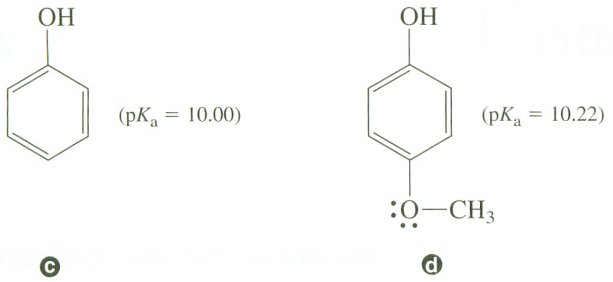
a) Explain why ⓑ is favored over ⓐ at equilibrium.

b) Show the structure of the conjugate base of ⓐ and explain how this isomerization reaction occurs.



ⓐ ⓑ

4.47 Compound **c** is a slightly stronger acid than compound **d**. The CH_3O group has both an inductive effect and a resonance effect on the acidity of **d**.



c **d**

a) Explain how the inductive effect of the CH_3O group should affect the acidity of **d**.

b) Show the resonance structures for **d** that involve the CH_3O group. Would you expect the resonance effect of the CH_3O group to cause an increase or decrease in acidity?

c) In situations like this, the resonance effect is usually larger than the inductive effect. Is this consistent with the experimental acidities of these two compounds?

4.48 Explain why the pK_a's of compounds near the middle of Table 4.2 are often listed with two figures to the right of the decimal place (that is, for NH_4^+ the pK_a = 9.24), whereas those at the beginning and end of the table are listed without any figures to the right of the decimal point (that is, for H_2SO_4 the $pK_a = -10$).

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4.49 For each pair of compounds, explain which is the stronger acid.

4.50 Explain why the compound on the left is a stronger acid than the compound on the right.

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